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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,783	09/28/2001	Stanko Bodnar	CRD-0967	5435

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EXAMINER	
CHORBAJI, MONZER R	
ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/966,783	BODNAR ET AL.	
	Examiner	Art Unit	
	MONZER R. CHORBAJI	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-26 and 28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-26 and 28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 Septemper 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/27/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This non-final action is in response to the amendment received on 12/12/07

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-5, 7-26 and 28-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 1, line 17; Applicant has added the limitation that each period of time ranging from about six hours to about seventeen hours. The disclosure as a whole does not teach this feature. The same applies to claim 20, line 22. The specification teaches several different predetermined time periods for each of a plurality of sterilization steps (i.e., preconditioning, sterilization, evacuation, degassing, etc.). However, nowhere in the specification does applicant teach a range of time periods which covers each of these predetermined periods.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-5, 7-10, 20-26, and 28-31are rejected under 35 U.S.C. 103(a) as being unpatentable over Muth et al (U.S.P.N. 5,472,702) in view of McGowan, Jr. (U.S.P.N. 5,749,203), Popescu et al (U.S.P.N. 5,464,580) and Mitchell (EP 0 568 310) as further evidenced by Sigma-Aldrich (biocompare.com Internet printout).

Regarding claims 1 and 20, Muth teaches the following: positioning a packaged (col.1, lines 19-24, col.2, lines 24-26 and col.5, lines 5-9), drug coated medical device in a sterilization chamber (col.7, line 38), increasing and maintaining the temperature in

the sterilization chamber in the range from 70-74 degrees Fahrenheit,a relative humidity in the range from 40%-50% for a predetermined time period (col.6, lines 43-46), injecting a sterilization agent at a predetermined concentration into the chamber and maintaining the temperature in the range from 75-140 degrees Fahrenheit, at a relative humidity in the range from 40%-70% for a predetermined time period (col.7, table, lines 54-59), and removing the sterilization agent from the chamber while maintaining the chamber at a temperature in the range of 87-93 degree Fahrenheit (col.7, table, Exhaust, lines 66-67 and col.6, lines 60-61) at a relative humidity of 30%.

More specifically, Muth teaches (Table in column 7, Exhaust section) applying two individual vacuum cycles in a chamber to the sterilized packages to remove residual ethylene oxide for time intervals of 20 minutes for each individual vacuum cycle. However, Muth further teaches (col.6, lines 57-64) that the time in the vacuum chamber is not limited to 20 minutes for each vacuum cycle. However, Muth does not teach removing sterilizing agent through a series of individual alternating vacuum and nitrogen washes at 30-40 degrees Celsius for 6 to 17 hours

Actually, the time in the vacuum chamber depends on the final desired removal amount of residual ethylene oxide. As such one of ordinary skill in the art would readily recognize that to achieve residual values of ethylene oxide for less than 220 ppm, a time interval of six hours or more per each individual vacuum cycle and also more than two vacuum cycles would ensure this final residual amount for the sterilant. It would have been obvious to one having ordinary skill in the art to modify the method of Muth to extend the sterilant evacuation period to whatever length necessary to remove all the

sterilant from the article being sterilized. It would have been obvious to one having ordinary skill in the art to determine, through routine experimentation, the optimum length of sterilant evacuation period in order to ensure sufficient sterilant removal.

Muth also does not specifically teach the following: applying another preconditioning step, creating vacuum, and using nitrogen washes steps where the time interval for each period of nitrogen wash ranges from about 6-17 hours.

McGowan teaches that preconditioning medical articles is known in the art of ethylene oxide sterilization (col.1, lines 26-27 and lines 36-44). More specifically, McGowan teaches that creating a vacuum (col.1, lines 52-64) and applying nitrogen rinses (col.2, lines 12-14) are also known conventional steps in this art (the two steps are considered individual and alternating). It would have been obvious to one of ordinary skill in the art at the time of the invention to further modify Muth method by including an additional preconditioning step since at elevated temperatures ethylene oxide gas is thought to be more molecularly active and therefore performs more effectively as a sterilizing agent as taught by McGowan (col.1, lines 36-40). It also would have been obvious to one having ordinary skill in the art to employ the nitrogen rinses, as taught by McGowan, in order to decrease flammability of the ethylene oxide (column 2, lines 12-17).

Deleted:

McGowan does not specifically teach time intervals for nitrogen washes. Popescu sterilizes medical items with ethylene oxide and further teaches of removing residual ethylene gas by adding nitrogen gas then evacuating the chamber (col.6, lines 20-33), because this approach results in the substantial removal of toxic ethylene oxide

gas from sterilized medical items (col.6, lines 12-15). Popescu teaches that the total time for the typical evacuation cycle is approximately 12 hours (col.6, lines 33-35). However, Popescu further teaches that the evacuation cycle is repeated for a number of cycles (col.6, lines 23-25). As such one of ordinary skill in the art would recognize that depending on the required amount of residual ethylene oxide in the sterilized medical items, the number of cycles varies.

As to the limitation that the drug coated on the medical device comprises a compound that inhibits mTOR and binds FKBP12 in claims 1-20, Muth discloses a method of sterilizing drug coated medical devices; however, it is unclear whether the drugs in Muth include a compound that inhibits mTOR and binds FKBP12.

Mitchell teaches it is known in the art to provide drug coated medical devices with a compound such as rapamycin in order to treat patients with vascular disease. The ability of Rapamycin to inhibit mTOR and to bind to FKBP12 is an inherent property as evidenced by the Sigma-Aldrich Internet printout. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify Muth method by sterilizing a drug coated medical device where the drug includes the compound in order to treat patients with vascular disease and further since rapamycin is known to inhibit transplantation rejection in mammals (page 3, numbered lines 12-13) making organ donations safer for recipients. It would have been obvious to sterilize any drug coated medical device with the modified method of Muth as it is effective and non-damaging to such devices.

Regarding claims 3, Muth teaches that the first predetermined period is three hours (col.6, lines 45-46). With respect to claims 7 and 28, Muth also teaches removing the sterilant from the packaged drug coated medical device (col.7, table, exhaust). With respect to claims 10 and 31, Muth teaches a biocompatible vehicle or coating that includes an agent in therapeutic dosages (col.8, lines 27-31).

Regarding claims 2, 4-5, 8-9, 21, 23-26 and 29-30, McGowan teaches some specifics of the ethylene oxide sterilization process which are not discussed in Muth. McGowan teaches the following: reducing the pressure in the chamber to under 10 kPa (col.10, lines 37-45); injecting gaseous ethylene oxide at a concentration from 200-1200 mg/l over a second predetermined period of 6 hours (col.2, lines 5-9); injecting ethylene oxide at a concentration from 800-950 mg/l over a second predetermined period of 6 hours (col.2, lines 5-9); removing the packaged drug coated medical device from the chamber and positioning it in a controlled environment (col.2, lines 18-22); circulating ambient air (col.2, lines 13-14); maintaining the temperature from 10-70 degrees Celsius (col.2, lines 21-22) over time period from 1hour-2 weeks (col.2, lines 64-65) or over time period from 12 hours-7 days (col.2, lines 64-65); and placing the packaged drug coated medical device in a preconditioning chamber (col.1, line 27); maintaining the temperature from 10-70 degrees Celsius (col.1, lines 31-32); and the relative humidity from 20%-95% (col.1, lines 32-33) over a time period of 1 hour-5 days (col.1, lines 34-35). It would have been obvious to one having ordinary skill in the art to modify Muth to use the specific parameters of concentration, exposure time and

temperature from McGowan, as McGowan teaches these are optimal and/or conventional in ethylene oxide sterilization of temperature sensitive materials.

Regarding claim 22, Muth, McGowan and Mitchell all do not specifically disclose a temperature range and a time interval as recited in the claim. Both Muth and McGowan disclose a relative humidity range value that falls within the recited range, for example, McGowan teaches preconditioning at a relative humidity from 40%-80% (col.1, lines 31-32). Popescu further teaches preconditioning at 25 degree Celsius for a time period from 60-90 minutes (col.5, lines 24 and 35-36). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Muth by adjusting the temperature range and the exposure time interval since such modifications is a matter of optimization as evidenced by Popescu.

7. Claims 11-13 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muth et al (U.S.P.N. 5,472,702) in view of McGowan, Jr. (U.S.P.N. 5,749,203), Popescu et al (U.S.P.N. 5,464,580) and Mitchell (EP 0 568 310) as further evidenced by Sigma-Aldrich (biocompare.com Internet printout) as applied to claims 10 and 20 and further in view of Rich (U.S.P.N. 6,025,414) and Pharriss et al (U.S.P.N. 3,675,647).

Regarding claims 11-12 and 32-34, Muth, McGowan, Popescu and Mitchell all do not specifically teach using the polymers poly (ethylene-co-vinyl acetate) and polybutylmethacrylate as coating material. Rich teaches that poly (ethylene-co-vinyl acetate) is incorporated into layers of implants (col.3, lines 36-37 and col.4, line 10). Therefore, it would have been obvious to one of ordinary skill in the art at the time the

invention was made to further modify composition of the medical devices coated in Muth to include the polymer poly (ethylene-co-vinyl acetate) as taught by Rich since it is known for it resiliency (col.4, lines 2-3).

Regarding claims 11-12 and 32-33, Rich fails to teach using the polymer polybutylmethacrylate. Pharriss teaches using polybutylmethacrylate (col.3, line 63). Thus, it would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify composition of the implants in Rich to include the polymer polybutylmethacrylate as taught by Pharriss since it is known to be biologically acceptable flexible, resilient, polymeric material (col.3, lines 59-60).

Regarding claims 13 and 34, Muth teaches incorporating the agent into the first layer (col.8, lines 28-30).

8. Claims 14-19 and 35-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muth et al (U.S.P.N. 5,472,702) in view of McGowan, Jr. (U.S.P.N. 5,749,203), Popescu et al (U.S.P.N. 5,464,580) and Mitchell (EP 0 568 310) as further evidenced by Sigma-Aldrich (biocompare.com Internet printout) as applied to claims 10, 20 and further in view of Gingras (WO 00/38754).

Regarding claims 14-19 and 35-40, Muth, McGowan, Popescu and Mitchell all do not specifically teach incorporating polyfluoro copolymers made up of first moiety and second moiety into medicated medical devices. Gingras teaches combining various biocompatible polyfluoro copolymers with polyfluoro monomers (page 10, lines 5-10) in coating layers for stent such that the coating layers are made of first and second moieties that is intrinsically combined in various concentration ranges. Also, Gingras the

use of hexafluoropropylene (page 10, line 10). As a result, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify composition of the coatings for medical devices in Muth to include hexafluoropropylene as taught by Gingras since such a compound is known to be biocompatible (page 10, line 5).

Response to Arguments

9. Applicant's arguments filed on 12/12/2007 have been fully considered but they are not persuasive.

On page 14 of the Remarks/Arguments section, Applicant argues that none of the references discloses the step of removing the sterilization agent from the sterilization chamber through a plurality of separate or individual alternating vacuum and nitrogen washes over a third predetermined period with the temperature in the range from about 30 ^{o}C to about 40 ^{o}C for the specific period of 6 to 17 hours in combination with the other steps. Examiner disagrees.

Muth teaches removing the sterilization agent from the chamber through a plurality of individual vacuum washes over another predetermined time period by maintaining the chamber at a temperature in the range of 30-40 degree Celsius (col.7, table, Exhaust, lines 66-67 and col.6, lines 60-61). More specifically, Muth teaches (Table in column 7, Exhaust section) applying a two individual vacuum cycles in a chamber to the sterilized packages to remove residual ethylene oxide for time intervals of 20 minutes for each individual vacuum cycle. However, Muth further teaches (col.6, lines 57-64) that the time in the vacuum chamber is not limited to 20 minutes for each

vacuum cycle, actually, the time in the vacuum chamber depends on the final desired removal amount of residual ethylene oxide. As such one of ordinary skill in the art would readily recognize that to achieve residual values of ethylene oxide for less than 220 ppm, a time interval of six hours or more per each individual vacuum cycle and also more than two vacuum cycles are required to achieve this final residual amount for the sterilant. Muth does not specifically teach applying nitrogen washes steps where the time interval for each period of nitrogen wash ranges from about 6-17 hours. McGowan teaches that creating a vacuum (col.1, lines 52-64) and applying nitrogen rinses (col.2, lines 12-14) are known conventional steps in this art (the two steps are considered individual and alternating). It would have been obvious to one of ordinary skill in the art at the time of the invention to further modify Muth method by including an additional preconditioning step since at elevated temperatures ethylene oxide gas is thought to be more molecularly active and therefore performs more effectively as a sterilizing agent as taught by McGowan (col.1, lines 36-40).

McGowan does not specifically teach time intervals for nitrogen washes. Popescu sterilizes medical items with ethylene oxide and further teaches of removing residual ethylene gas by adding nitrogen gas then evacuating the chamber (col.6, lines 20-33), because this approach results in the substantial removal of toxic ethylene oxide gas from sterilized medical items (col.6, lines 12-15). Popescu teaches a typical cycle is made up of two separate cycles where each of the two cycles has two steps. The first step in this cycle is adding nitrogen (this step is considered nitrogen wash as recited in the claims) and the second step is evacuating where this second step occurs over

approximately 120 minutes (col.6, lines 25-28). The second cycle in the typical cycle is again made up of two cycles where each of the two cycles has two steps. The first step in this second cycle is reintroducing nitrogen and circulating the nitrogen for approximately 90 minutes and the second step is evacuating the chamber over a period of approximately 100 minutes and maintaining that pressure for additional 240 minutes (col.6, lines 29-33). Popescu further teaches that the total time for the typical cycle which is made up of two cycles is approximately 12 hours (col.6, lines 33-35). However, Popescu further teaches that the number of cycles of adding nitrogen then evacuating is repeated for a number of cycles (col.6, lines 23-25). As such one of ordinary skill in the art would recognize that depending on the required amount of residual ethylene oxide in the sterilized medical items, the number of cycles varies. It would have been obvious to one of ordinary skill in the art at the time of the invention to further add a series of nitrogen washing steps to Muth's method, because the combination of nitrogen washes and vacuum washes result in the substantial removal of toxic ethylene oxide gas from sterilized medical items as explained by Popescu (col.6, lines 12-15).

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MONZER R. CHORBAJI whose telephone number is (571)272-1271. The examiner can normally be reached on M-F 9:00-5:30.

11. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. R. C./

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797

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